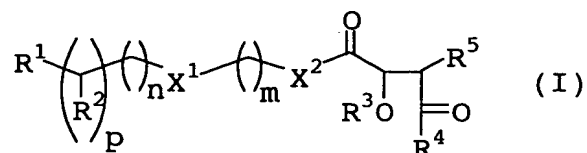
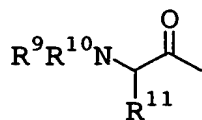


Claims

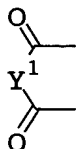
1. A proteasome inhibitor comprising, as an active ingredient, a carboxylic acid derivative represented by the formula (I) or a pharmaceutically acceptable salt thereof:



<wherein m and n are the same or different and represent an integer of 0 to 10; p represents 0 or 1; R¹ represents a hydrogen atom, substituted or unsubstituted alkyl, substituted or unsubstituted alicyclic alkyl, substituted or unsubstituted aralkyl, substituted or unsubstituted aryl or NR⁶R⁷ {wherein R⁶ represents a hydrogen atom, substituted or unsubstituted alkyl, or substituted or unsubstituted aralkyl, and R⁷ represents a hydrogen atom, substituted or unsubstituted alkyl, substituted or unsubstituted aralkyl, CW¹R⁸ (wherein R⁸ represents a hydrogen atom, substituted or unsubstituted alkyl, substituted or unsubstituted alkylamino, substituted or unsubstituted alkoxy, substituted or unsubstituted aryl, a substituted or unsubstituted heterocyclic group, substituted or unsubstituted aralkyl, substituted or unsubstituted aralkylamino, or substituted or unsubstituted aralkyloxy, and W¹ represents an oxygen atom or a sulfur atom), or the formula:

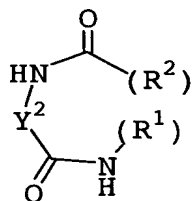


(wherein R^9 represents a hydrogen atom, substituted or unsubstituted alkyl, or substituted or unsubstituted aralkyl; R^{10} represents a hydrogen atom, substituted or unsubstituted alkyl, substituted or unsubstituted aralkyl, CW^2R^{8a} (wherein R^{8a} and W^2 have the same significances as the above R^8 and W^1 , respectively), substituted or unsubstituted alkylsulfonyl, substituted or unsubstituted arylsulfonyl, or PW^3R^{12} , (wherein R^{12} 's are the same or different and represent substituted or unsubstituted alkyl, or substituted or unsubstituted aryl; and W^3 has the same significance as the above W^1); or R^9 and R^{10} together represent the formula:



(wherein Y^1 represents substituted or unsubstituted alkylene or substituted or unsubstituted arylene); and R^{11} represents a hydrogen atom, substituted or unsubstituted alkyl, or substituted or unsubstituted aralkyl); R^2 represents a hydrogen atom, COR^{13} (wherein R^{13} represents hydroxy, substituted or unsubstituted alkoxy, substituted or unsubstituted alkenyloxy, substituted or unsubstituted aralkyloxy, substituted or unsubstituted alicyclic alkylalkoxy, substituted or unsubstituted aroylalkoxy, or $\text{NR}^{14}\text{R}^{15}$ (wherein R^{14} represents

a hydrogen atom, substituted or unsubstituted alkyl, or substituted or unsubstituted aryl; and R^{15} represents substituted or unsubstituted alkyl, substituted or unsubstituted aralkyl, substituted or unsubstituted alkoxycarbonylalkyl, amino, substituted or unsubstituted alkylamino, or substituted or unsubstituted arylamino; or R^{14} and R^{15} together with the adjacent N form a substituted or unsubstituted heterocyclic group)) or CH_2OR^{3a} (wherein R^{3a} represents a hydrogen atom, substituted or unsubstituted alkyl, substituted or unsubstituted aralkyl, substituted or unsubstituted alkanoyl, substituted or unsubstituted aroyl, or SiR^{16}_3 (wherein R^{16} 's are the same or different and represent substituted or unsubstituted alkyl, or substituted or unsubstituted aryl)); or R^1 and R^2 together represent the formula:

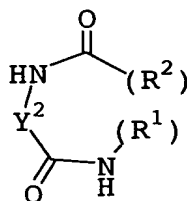


(wherein Y^2 represents substituted or unsubstituted alkylene); X^1 represents a bond, substituted or unsubstituted alkylene, substituted or unsubstituted alicyclic alkylene, substituted or unsubstituted alkenylene, or substituted or unsubstituted arylene; X^2 represents an oxygen atom, a sulfur atom or NR^{17} (wherein R^{17} represents a hydrogen atom, substituted or

unsubstituted alkyl, or substituted or unsubstituted aralkyl); R^3 has the same significance as the above R^{3a} ; R^4 represents hydroxy, mercapto, substituted or unsubstituted alkoxy, or substituted or unsubstituted alkylthio; or R^3 and R^4 together represent a bond; and R^5 represents a hydrogen atom, substituted or unsubstituted alkyl, substituted or unsubstituted alkenyl, or substituted or unsubstituted aralkyl>.

2. The proteasome inhibitor according to claim 1, wherein R^3 and R^4 together represent a bond.

3. The carboxylic acid derivative or the pharmaceutically acceptable salt thereof according to claim 1, wherein R^4 is hydroxy, or substituted or unsubstituted alkoxy; p is 1; R^1 is a hydrogen atom or NR^6R^7 (wherein each of R^6 and R^7 has the same significance as defined above), or R^1 and R^2 together are the formula:



(wherein Y^2 has the same significance as defined above); X^1 is substituted or unsubstituted alicyclic alkylene, or substituted or unsubstituted arylene; and X^2 is NR^{17} (wherein R^{17} has the same significance as defined above).

4. The carboxylic acid derivative or the pharmaceutically acceptable salt thereof according to claim

1, wherein R^4 is mercapto, or substituted or unsubstituted alkylthio, or R^3 and R^4 together are a bond; X^2 is NR^{17} (wherein R^{17} has the same significance as defined above)[when m is 0; n and p are 1; R^2 is carboxy; R^3 and R^4 together are a bond; R^5 is sec-butyl; and X^1 is cyclopropylene or ethylene, R^1 is neither $NHC(=O)-C(CH_3)NH_2$ nor $NHC(=O)-C(CH_3)NHC(=O)O-C(CH_3)_3$].

5. The carboxylic acid derivative or the pharmaceutically acceptable salt thereof according to claim 3, wherein R^1 is a hydrogen atom or NR^6R^7 (wherein each of R^6 and R^7 has the same significance as defined above).

6. The carboxylic acid derivative or the pharmaceutically acceptable salt thereof according to ~~claim 5~~, wherein R^1 is NR^6R^7 (wherein each of R^6 and R^7 has the same significance as defined above); X^1 is cyclopropylene or alkylene; and X^2 is NH.

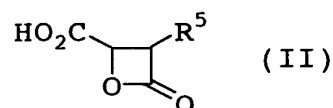
7. The carboxylic acid derivative or the pharmaceutically acceptable salt thereof according to claim 4, wherein R^4 is mercapto, or substituted or unsubstituted alkylthio; R^1 is NR^6R^7 (wherein each of R^6 and R^7 has the same significance as defined above); and X^1 is cyclopropylene or alkylene.

8. The carboxylic acid derivative or the pharmaceutically acceptable salt thereof according to ~~claim 4~~, wherein R^3 and R^4 together are a bond.

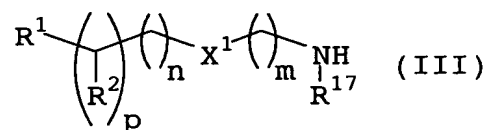
9. The carboxylic acid derivative or the

pharmaceutically acceptable salt thereof according to claim 8, wherein m is 0; n and p are 1; R¹ is NR⁶R⁷ (wherein each of R⁶ and R⁷ has the same significance as defined above); R² is COR^{13a} (wherein R^{13a} is alkylamino, aralkyloxy or aralkylamino); R⁵ is alkyl; X¹ is cyclopropylene, alkylene, or substituted or unsubstituted phenylene; and X² is NH.

10. A process for producing the carboxylic acid derivative according to claim 1, wherein R³ and R⁴ together represent a bond and X² is NR¹⁷, characterized in that a carboxylic acid represented by the formula (II):



(wherein R⁵ has the same significance as defined above) is reacted with an amine represented by the formula (III):

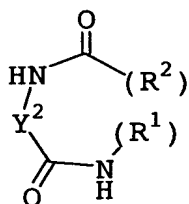


(wherein each of m, n, p, R¹, R², R¹⁷ and X¹ has the same significance as defined above).

11. The carboxylic acid according to claim 10, wherein R⁵ is substituted or unsubstituted alkyl, substituted or unsubstituted alkenyl, or substituted or unsubstituted aralkyl, or a salt thereof.

12. The amine according to claim 10, wherein m is 0; n and p are 1; R¹ is NR⁶R⁷ (wherein each of R⁶ and R⁷ has the same significance as defined above); R² is COR¹³ (wherein R¹³

has the same significance as defined above) or $\text{CH}_2\text{OR}^{3a}$ (wherein R^{3a} has the same significance as defined above), or R^1 and R^2 together are the formula:



(wherein Y^2 has the same significance as defined above); and X^1 is cyclopropylene, or a salt thereof.

13. The amine or the salt thereof according to claim 12, wherein R^1 is amino and R^{17} is a hydrogen atom.

14. The amine or the salt thereof according to claim 13, wherein R^2 is carboxy.

15. A pharmaceutical composition comprising the amine or the salt thereof according to any one of claims 12 to 14 as an active ingredient.

16. A compound wherein the amine according to any one of claim 12 to 14 is protected with a protecting group, or a salt thereof.

17. A pharmaceutical composition comprising the carboxylic acid derivative or the pharmaceutically acceptable salt thereof according to any one of claims 3 to 9 as an active ingredient.

18. A proteasome inhibitor comprising the carboxylic acid derivative or the pharmaceutically acceptable salt thereof

according to any one of claims 3 to 9 as an active ingredient.

19. An antitumor agent comprising the carboxylic acid derivative or the pharmaceutically acceptable salt thereof according to any one of claims 3 to 9 as an active ingredient.

20. A pharmaceutical composition comprising the carboxylic acid derivative or the pharmaceutically acceptable salt thereof according to any one of claims 3 to 9 as an active ingredient, used for the treatment of the diseases curable by proteasome inhibition.

21. A use of the carboxylic acid derivative or the pharmaceutically acceptable salt thereof according to any one of claims 3 to 9 for the manufacture of a proteasome inhibitor.

22. A use of the carboxylic acid derivative or the pharmaceutically acceptable salt thereof according to any one of claims 3 to 9 for the manufacture of an antitumor agent.

23. A method to inhibit proteasome comprising a process in which an effective amount of the carboxylic acid derivative or the pharmaceutically acceptable salt thereof according to any one of claims 3 to 9 is administered to a mammal including human.

24. A method of treatment or prevention of a tumor comprising a process in which an effective amount of the carboxylic acid derivative or the pharmaceutically acceptable salt thereof according to any one of claims 3 to 9 is administered to a mammal including human.